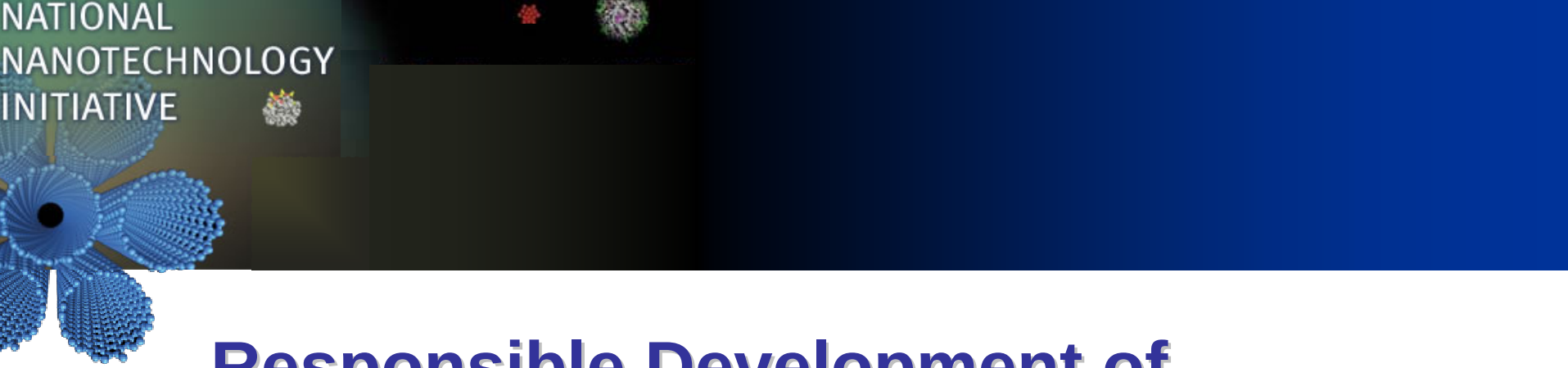


Responsible Development of Nanotechnology

National Nanotechnology Initiative Meeting
April 2, 2004

E. Clayton Teague
Director
National Nanotechnology Coordination Office
Nanoscale Science, Engineering, and Technology Subcommittee
Committee on Technology
National Science and Technology Council

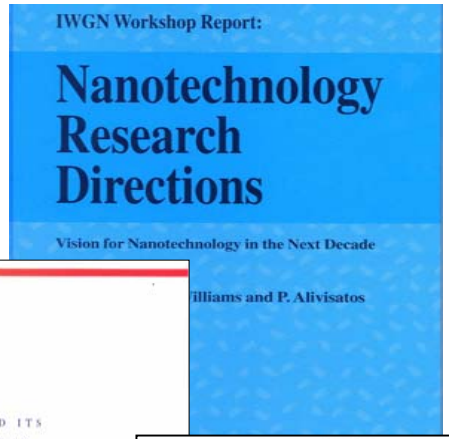
National Nanotechnology Initiative - NNI

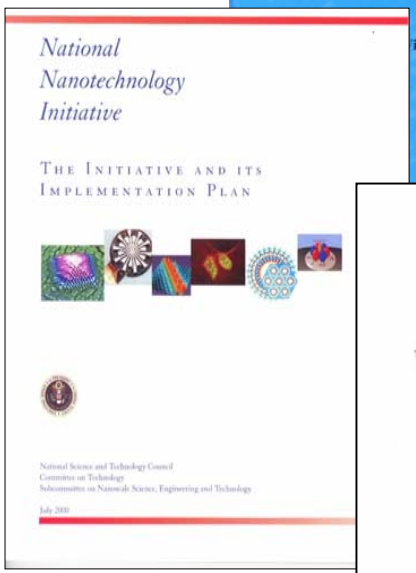
Fully realize the promise of nanotechnology and translate that promise into improvements in the Nation's economy, national security, and quality of life…

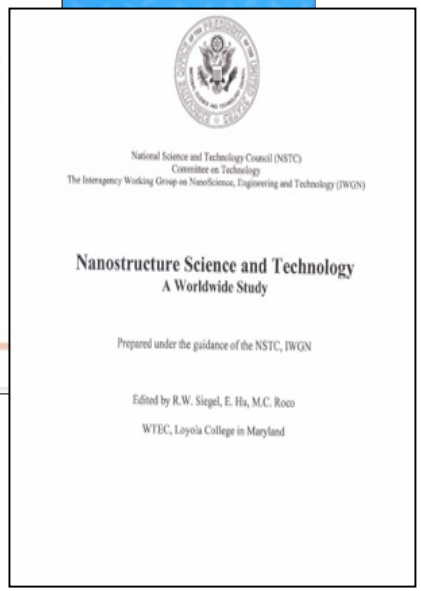
…while protecting public health and the environment

Planning the NNI

1999: 10-year vision

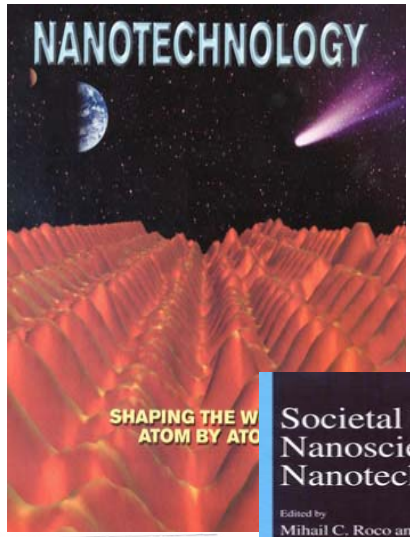






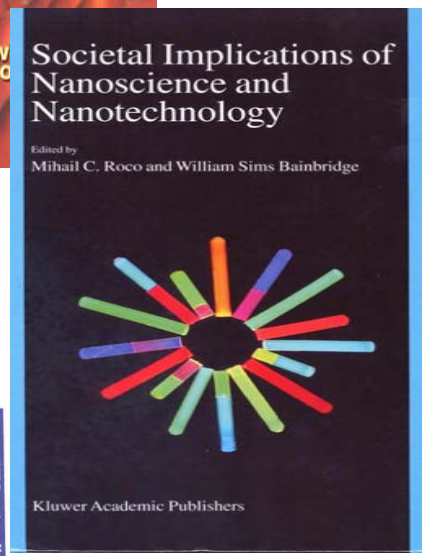
Government plan

Reports



Brochure for public

Societal implications



Worldwide benchmark

MC. Roco, 5/08/03

Workshops/conferences on nano-environmental research: examples

- NSF, 6/2002: "Nanoparticles and the environment" (grantees meeting)
- EPA, 11/2002: "Nanotechnology and the environment applications and implications" (grantees meeting)
- ACS, 3/2003: Symposium on nanotechnology implications in the environment, New Orleans
- NNI, 5/2003: Vision for environmental implications and improvement (at NSF)
- NNI, 9/2003: Interagency grantees meeting (at NSF)

Main Points of Talk

- Existing Federal regulatory mechanisms are in place for assessing and regulating workplace, environmental, and health risks of new technology materials
- Active efforts are underway to ensure that these regulatory mechanisms or appropriately amended ones provide proper coverage of nanotechnology-based materials
- Research in Federal laboratories, private industry, and academia is now in progress to determine how the nanotechnology-based materials may differ from conventional ones in their implications for public health and the environment

Nanoscale Materials Categorizations

- **Naturally occurring "ultrafine particles"**
  - *Virus – 10 nm to 60 nm*
  - *Bacteria – 30 nm to 10 μm*
  - *Dust from deserts - ~100 nm*
  - *Volcanic ash, Forest fire smoke*
- **"Ultrafine particles" from established technologies or by-products of conventional processes**
  - *Combustion soot – 10 nm to 80 nm*
  - *Paint pigments – 80 nm to 100 nm*
  - *Welding fumes – 10 nm to 50 nm*
  - *Diesel exhaust particles – (small mode) 7 nm to 40 nm*
  - *Carbon black for photocopier toner – 10 nm to 400 nm*
- **Engineered nanoscale materials – "nanomaterials"**
  - *Fullerenes - buckyballs – 1 nm; nanotubes – 1 nm to 5 nm X 10 μm*
  - *Quantum dots – 5 nm to 20 nm*
  - *Semiconductor wires*

Current Commercial "Nanomaterials"

- **Metal oxides**
  - Ceramics from oxides of zinc, iron, cerium, and zirconium
  - Chemo-mechanical polishing agents for semiconductor wafers
  - Scratch resistant coatings for glass
  - Cosmetics and sunscreens
- **Nanoclays**
  - Naturally occurring plate-like clay particles
  - Improve strength, hardness, heat resistance and flame retardancy of materials
  - Step assist on automobiles, barrier films in plastic beverage bottles, paper juice cartons and tennis balls
- **Nanotubes**
  - Coatings to dissipate and minimize static electricity – fuel lines, hard disk drive handling trays
  - Electrostatically paintable car exterior components
  - Flame retardant fillers for plastics
  - Field emitter sources in flat panel displays (exploratory)
- **Quantum Dots**
  - Medical diagnostics and therapeutics (exploratory)
  - Self assembly of nanoelectronic structures (exploratory)

Ultrafine Particles: Toxicology

- Large body of research on toxicity of ultrafines
  - Recent examination of literature indicated over 10,000 peer-reviewed papers – Vicki Colvin
  - Ambient ultrafine particles are associated with adverse respiratory and cardiovascular effects in susceptible people
  - Leading to safety and health regulations in some industries such as welding, smelting, beryllium
- Some of most recent work on toxicity, fate, and transport of PTFE, metal, metal oxide, and carbon ultrafine particles in animals
  - University of Rochester (G. Oberdorster)
  - Raised concern about UFP crossing blood-brain barrier

Engineered Nanomaterials: Toxicology

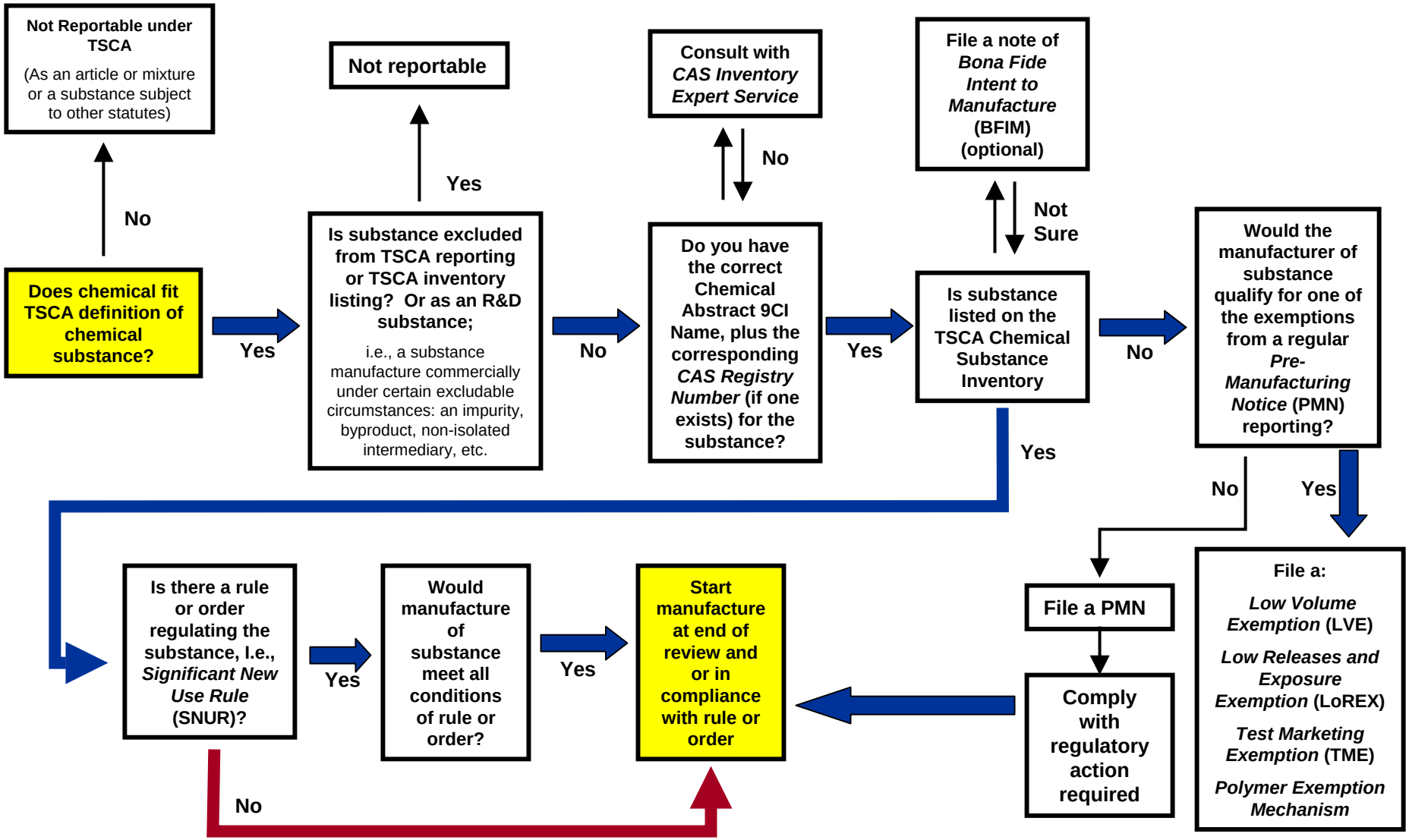
- **Lung instillation of single walled carbon nanotubes (Lam, Warheit 2003)**
  - SWNT engendered different tissue response than ultra-fine carbon
  - Materials were not cleared by macrophages
  - SWNT have low respirable levels in air (NIOSH study)
- **Quantum dot toxicity in cell culture (Bhatia 2004)**
  - Cadmium selenide dots were phototoxic to cells
- **Fullerenes in animals and cell cultures (~20 papers 2003-2004)**
  - Disagreements in data from different laboratories
  - Generally, fullerenes are photoxic species
  - Diversity of surface coatings makes comparisons challenging

From Vicki Colvin, Rice University

Relevant Existing Regulatory Standards

- **Production of industrial chemicals & particulates and their possible introduction into air, water, or soil**
  - Toxic Substance Control Act (TSCA) of 1976 – administered by EPA
    - Track over 75,000 chemicals produced or imported into US
  - Clean Air Act for particulate matter <10 μm (PM10) in force - coarse;
  - Clean Air Act for particulate matter <2.5 μm (PM2.5) - fine
    - Put into effect in 1997, data gathering from 1999 to 2003, data analysis and deliberations about regulations underway
- **Materials in workplace governed by aerosol-based standards and ultrafine particle standards with**
  - Recommended exposure limits (RELs) established by NIOSH
  - Permissible exposure limits (PELs) established by OSHA
  - Threshold limit values (TLVs) established by American Conference of Government Industrial Hygienists (ACGIH)
  - Regulations for personal protective equipment to reduce exposures set by OSHA, NIOSH and ASTM
  - Based on existing health risk data
  - Targeted at vulnerable regions of the respiratory system

Processing New Chemical Through TSCA



Based on Chart by Ahson Wardak – UVA; Reviewed by EPA

Relevant Existing Regulatory Standards

- **Foods and food packaging - FDA and USDA share in regulations for food safety**
  - FDA – fish, shellfish, animal feeds
  - USDA – processed meat & meat products
- **Food additives, pharmaceuticals to be metabolized by human body – regulated by FDA**
  - All “drugs,” food additives, food coloring must have pre-market approval by FDA – called a New Drug Application (NDA)
  - Sunscreen with specified SPF considered a drug
- **Diagnostic or therapeutic medical devices – regulated by FDA**
  - Regulatory path for quantum dots has not been determined
- **Substances incorporated into consumer products – regulated by CPSC under Federal Hazardous Substance Act**
  - No pre-market certification or approval
  - Control of use of substance in product determined by risk of exposure

Main Points of Talk

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Organized Focus Group

- **Interagency Group on health and environmental impacts of nanomaterials**
- **Membership from all relevant regulatory and research agencies, OSTP, and OMB**
- **Goals of Group:**
  - Serve as communication channel for information about regulatory work on nanomaterials by all involved agencies
  - Identify any major issues that require individual agency or cross-agency actions
  - Examine coverage of production and use of nanomaterials by existing regulatory mechanisms
  - Develop and issue through NIOSH a “best practices” document for working with nanomaterials
  - Work with industry and academia to develop nomenclature for nanomaterials
- **Convened in August 2003 by NNCO in coordination with OSTP**

Problem Coverage Areas

- **Lack of nomenclature for identifying and delineating nanomaterials**
- **Nanomaterials of same chemical but having different forms**
  - E.g., carbon black, diamond, buckyball, nanotube
- **Nanomaterials of same chemical but differing only by physical size**
  - E.g., TiO_2, quantum dots (CdS or CdSe)
- **No documentation of recommended "best practices" for working with the nanomaterials**

Nanomaterials Nominated to NTP

- **Nominated by:** V.Colvin, ***Rice University Center for Biological and Environmental Nanotechnology in May 2003***
- ***Nominated for:*** ***Toxicological characterization of several representative classes of nanomaterials***
- **Rationale for nomination:** ***Intense current and anticipated future research and development focus; further studies and development of appropriate toxicological methods are needed to adequately assess health effects***
- ***Testing recommendations:*** ***Toxicological studies:***
  - *Size- and composition-dependent biological disposition of nanocrystalline fluorescent semiconductor materials*
  - *Toxicological characterization of high aspect ratio carbon nanomaterials*
  - *Role of particle core and surface composition in the immunotoxicity of the above listed materials*
  - *Phototoxicity of representative metal oxide nanoparticles*

Established in 1978 by Department of Health and Human Services

- ***to coordinate toxicological testing programs within the Department,***
- ***strengthen the science base in toxicology***
- ***develop and validate improved testing methods***
- ***provide information about potentially toxic chemicals to***
  - health regulatory and research agencies
  - the scientific and medical communities
  - the public

NTP Organization

NTP Director
Dr. K. Olden, Dir NIEHS

Policy Oversight

Executive Committee

ATSDR	NCI/NIH
CPSC	NIEHS/NIH
EPA	OD/NIH
FDA	NIOSH/CDC
NCEH/CDC	OSHA

Environmental Toxicology Program

External Science Oversight and Peer Review

Board of Scientific Counselors

Scientific Advisory Committee On Alternative Toxicological Methods

NIEHS

NCTR
National Center for Toxicological Research
U.S. Food and Drug Administration

NIOSH

Status of NTP Project for Nanomaterials

- Nomination approved by NTP review in October 2003
- Initial planning of studies at the NTP to determine the toxicity of nanomaterials is under way with funding committed to begin several projects in FY04
- Funding for these studies to be ramped up to $5M/yr by FY08
- Studies will begin with distribution and uptake by skin of titanium oxide, several types of quantum dots, and then fullerenes
- NTP is also considering conducting inhalation studies of fullerenes

Main Points of Talk

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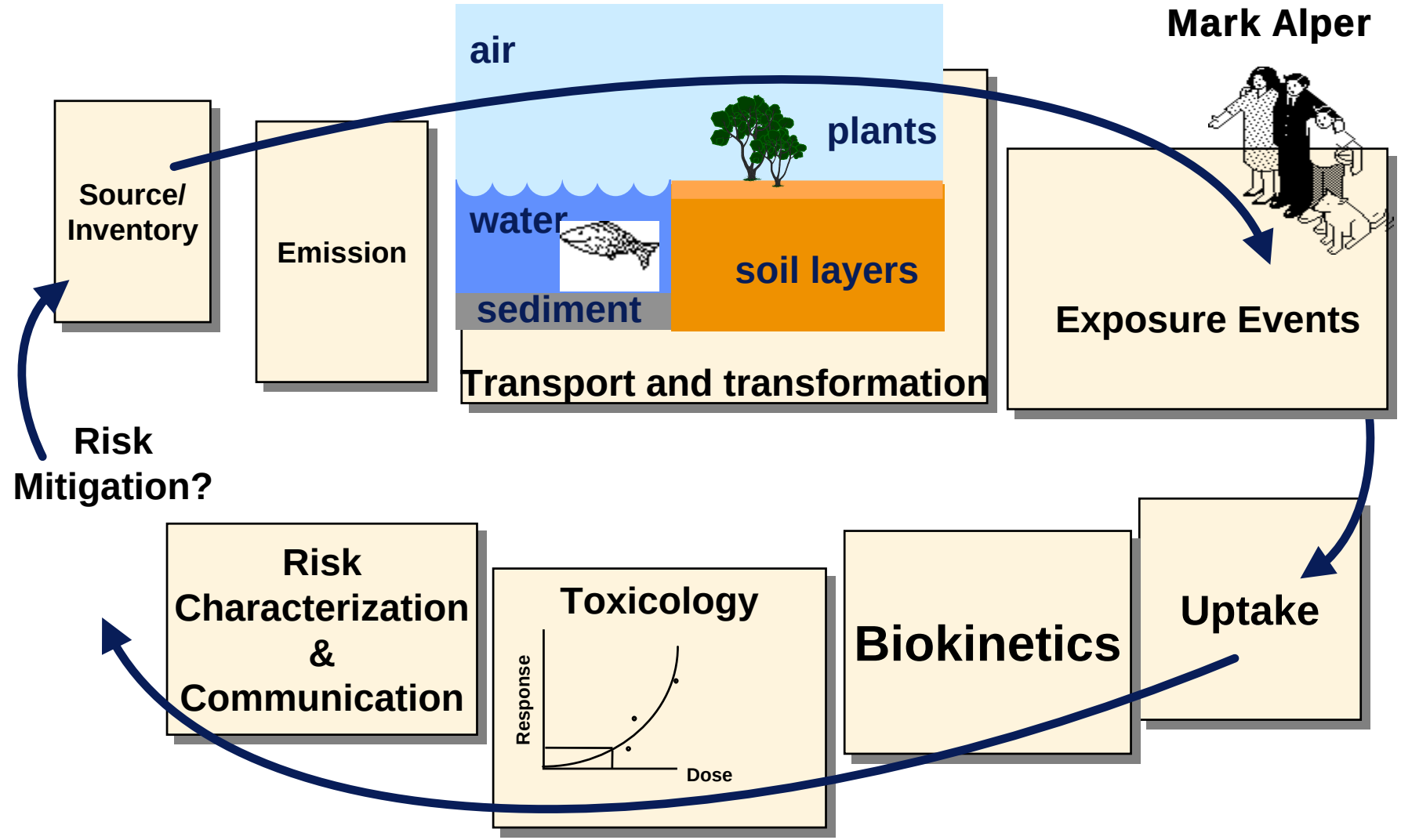
Source-to-Dose/Risk

DOE Molecular Foundry—Lawrence Berkeley National Laboratory

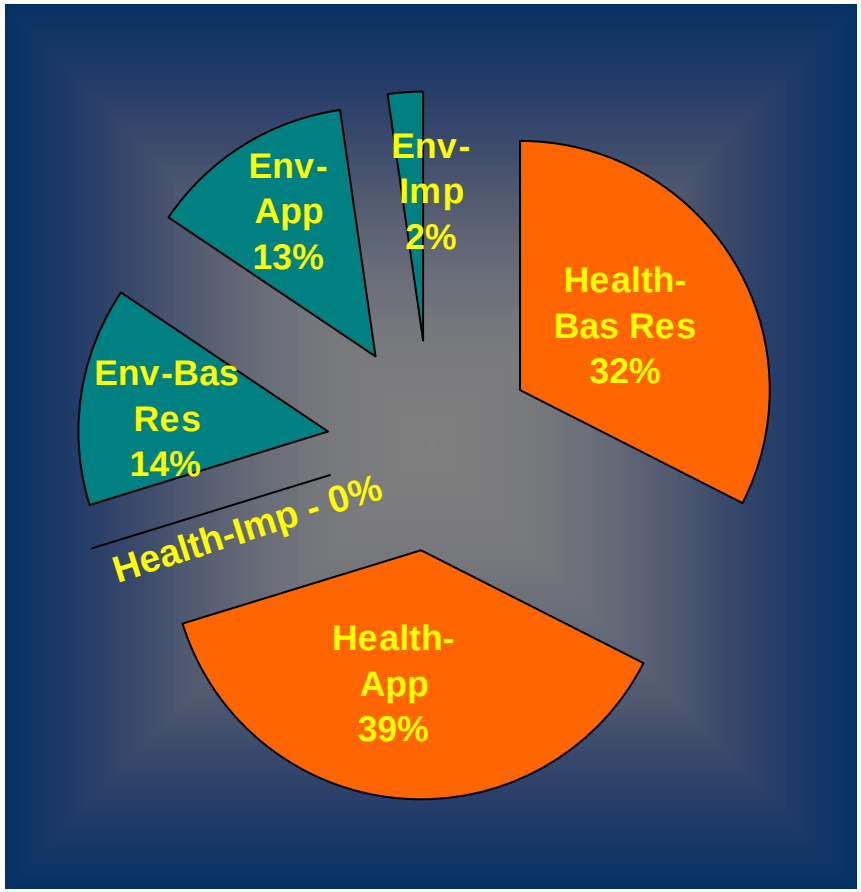
Mark Alper



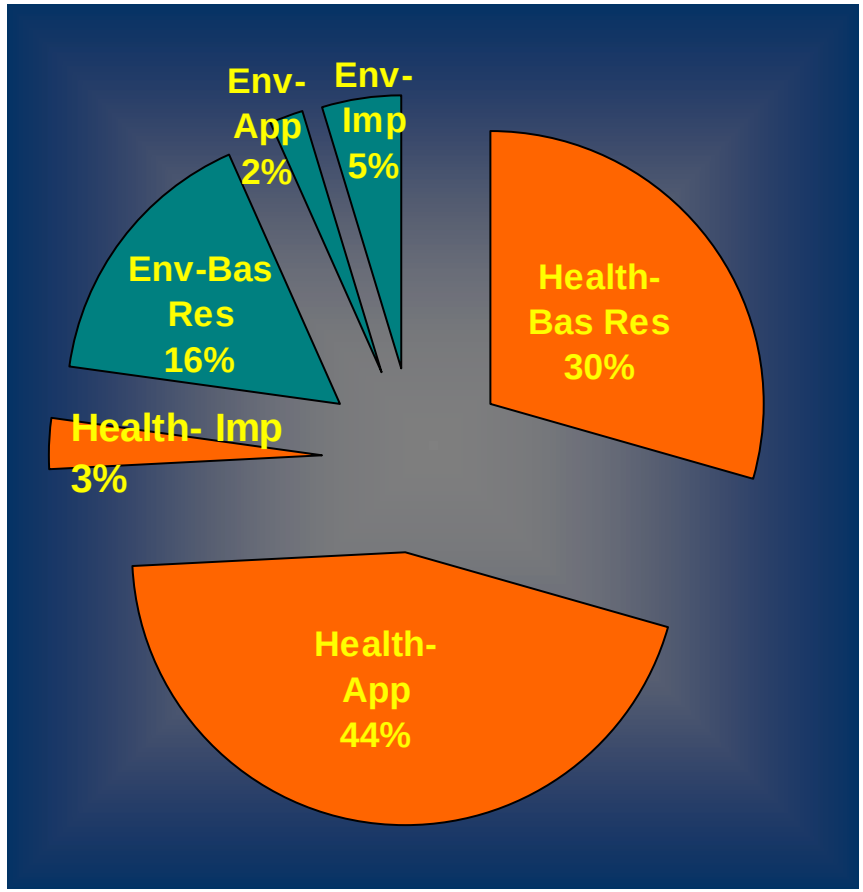
NNI R&D Funding for Health & Environment

- **Basic Research *(Examples)***
  - Fundamental investigations of chemistry, biology, and physics of nanoscale material interactions at the molecular and cellular level addressed in *in vitro* experiments and models. The information will lead to better understanding of these interactions in the body
  - Fundamental investigations of nanoscale materials interactions with air, water, soil, and chemicals
- **Applications *(Examples)***
  - Diagnostic and therapeutic methods; *in vivo* imaging; novel drug delivery
  - Methods for environmental remediation
  - Instrumentation for measurement and characterization
  - Miniaturized, high sensitivity and high selectivity sensors
- **Implications *(Examples)***
  - Programs focused on the toxicity of ultrafine and nanoparticles
  - Studies to determine health risks associated with inhalation and dermal exposure to nanoscale materials
  - Transport and fate of nanoscale materials in the environment

NNI R&D Funding for Health & Environment



2001 Total Funding for R&D Related to Health and Environment
$55.5M = 12% of NNI Funding - $464M



2004 Total Funding Estimated for R&D Related to Health and Environment
$105.8M = 11% of NNI Funding - $961M

Qualifications of Funding Charts

- Most of the agencies do not "budget" in the defined categories – thus funding values are estimates
- Partitioning into basic research, applications and implications has been estimated from the aims of specific research projects
- Some of the estimates for implications may change the ratio between health and the environment as awards are made later in the year

Specific Projects On Implications

- **NIH / NIEHS – support of the new National Toxicology Program, ~$3M multi-year project initiated in FY2004**
  - Studies to evaluate the toxic and carcinogenic potential of test agents (inc. quantum dots & nanotubes) in laboratory animals via inhalation exposure
- **EPA – Impacts of manufactured nanomaterials on human health and the environment, ~$4M in FY2004**
  - Toxicology of manufactured nanomaterials
  - Fate, transport, and transformation of manuf. nanomaterials
  - Human exposure and bioavailability
- **DOE Molecular Foundry at Lawrence Berkeley Nat. Lab.**
  - User facilities now open to support research by users on environmental and health effects
  - Transport and transformation of nanoparticles in the environment – air; water; within organisms – chemistry, exposure, risk analysis
  - Effects of nanomaterials on cell pathways and oxidative damage on gene expression

R&D Underway Funded by Agencies

- **NSF -$16M in basic research for environment; $36M counting cross-cut projects**
  - Nanoparticles in the environment; UC Davis & UMinn
  - Nanostructures in the environment: UCB & Texas Tech
  - Molecular materials – Microbial interactions w/environment: UOK & UVA
  - Biological and Environmental Engineering NSEC: Rice
- **FDA**
  - Internal R&D on regulatory issues as they arise
- **DOD - $1M+ in FY2004**
  - 6.2 project to investigate toxicity of nanoparticle munitions in collaboration w/ &DOE/ORNL
  - 6.1 project to look at potential bio-effects of nano-energetic particles in collaboration w/ &DOE/ORNL
  - In FY04; plans to invest $1M/yr in MURI program to investigate interaction of nanomaterials and cellular responses

R&D Underway Funded by Agencies

- **NIOSH - $1.5M across all three health subcategories**
  - Convenor of ISO WG developing guidelines for UFP exposure characterization
  - About 20 researchers focusing in part on nanotubes and Qdots and underlying toxicology, risk assessment, and exposure monitoring
- **NIST - $630K in environmental applications**
  - Development of standards and measurements for nanoscale particles
- **NIH – Total $80M**
  - $30M – Basic research – fundamental studies at the nanoscale of how molecules and assemblies of molecules work in cells
  - $47M – Applications – Broad range from instrumentation development to tissue engineering to developing methods for modifying nanoparticles for in vivo imaging (for cells in culture and in intact animals).

Other Efforts of NNI Related to EH R&D

- **NSF funds additional projects in crosscut areas that overlap with environmental basic research; $7M in 2001 and $20M in 2004**
- **DOD has $20M/yr for Chemical, Biological, Radiological, and Explosive protection/detection that has relevance to environment & health**
- **NASA invests ~ $2.0M/yr on measurements of atmospheric constituents**
- **EPA supports research on ultrafines at two particulate matter research centers at a total level of $2M/yr**
  - Rochester PM Center (Gunther Oberdorster) ~$1.5 M/year--all directed toward research on ultrafines
  - Southern California Particle Center and Supersite (John Froines) ~$0.5 M/year on ultrafine particles--about a third of the Center's research efforts